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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 10/672,397 | 09/26/2003 | Qinghong Yang | 26757-718.301 | 1830 |
| 21971 | 7590 | 04/05/2006 | EXAMINER | |
| WILSON SONSINI GOODRICH & ROSATI 650 PAGE MILL ROAD PALO ALTO, CA 94304-1050 | | | LU, FRANK WEI MIN | |
| | | ART UNIT | PAPER NUMBER | |
| | | 1634 | | |

DATE MAILED: 04/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) |
|------------------------------|------------------------|---------------------|
| | 10/672,397 | YANG ET AL. |
| Examiner | Art Unit | |
| Frank W. Lu | 1634 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 26 September 2003.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-18 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-18 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.

10) The drawing(s) filed on 9/26/2003 is/are: a) accepted or b) objected to by the Examiner.

 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 9/03 and 11/05.
4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
5) Notice of Informal Patent Application (PTO-152)
6) Other: ____.

DETAILED ACTION

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because provisional application 60/188,699 should be 60/188,669.

Specification

2. The amendment filed September 26, 2003 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material “the content of US application 09/804,661 is incorporated herein by reference in their entireties” in the first sentence of the specification is not supported by the original disclosure because there are no US application 09/804,661 in the first sentence of the specification in the original disclosure.

Applicant is required to cancel the new matter in the reply to this Office Action.

3. The disclosure is objected to because of the following informalities: since case 09/804,661 now is US Patent No. 6,653,079 B2, applicant is required to update this information in the first sentence of the specification.

Appropriate correction is required.

Claim Objections

4. Claims 1 and 16 are objected to because of the following informality: no period should appear after the label of each step, e.g., "a." should be --a--.
5. Claim 10 is objected to because of the following informality: (1) there should be no "and" between Ccel and SpCcel; and (2) there should be "and" between SpCcel and Hjc.
Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Enablement

Claims 1-9 and 11-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for performing the method recited in claim 1 by binding of a first reagent that selectively binds four junctions together in a four-way complex, does not reasonably provide enablement for the method recited in claim 1 by binding of a first reagent that binds any part in a four-way complex. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the

quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance in the specification to show that the method recited in claim 1 can be performed by binding of a first reagent that binds any part in a four-way complex. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether the method recited in claim 1 can be performed by binding of a first reagent that binds any part in a four-way complex.

Claim 1 is directed to a method for detecting the presence of a difference between two related polynucleotide sequences. The specification does not provide a guidance to show that the method recited in claim 1 can be performed by binding of a first reagent that selectively binds four junctions together in a four-way complex wherein the first reagent is selected from the group consisting of RuvA, RuvC, RuvB, RusA, RuvG, Ccel and spCcel, and Hjc. Since it is known in the art that some dye such as ethidium bromide can bind to double stranded nucleic acid (see page 161 of Maniatis et al., Molecular Cloning: A Laboratory Manual, 1982) and claim 1 does not limit the first reagent as a reagent that selectively binds four junctions together in a four-way complex, when the first reagent is ethidium bromide, detecting the signal produced upon the specific binding of said first reagent to said four-way complex cannot be used as indicative of the presence of said four-way complex and the signal thereof being related to the presence of said difference between said nucleic acid sequences as recited in step d) of claim 1 because

ethidium bromide can bind both the four-way complex and a double stranded nucleic acid and cannot be used to distinguish the four-way complex from a double stranded nucleic acid. Furthermore, since either a first reagent or said four-way complex in step c) of claim 1 do not label with a dye and said first or second reagent or said four-way complex in step a) of claim 16 do not label with a dye, it is unclear how to produce a detectable signal as recited in claims 1 and 16.

With above unpredictable factor, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether the method recited in claim 1 by binding of a first reagent that selectively binds any part in a four-way complex.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 1 recites the limitation "said nucleic acid sequences" in step b) of the claim. There is insufficient antecedent basis for this limitation in the claim because step a) of the claim only has polynucleotide sequences. Please clarify.

11. Claim 1 is rejected as vague and indefinite in view of the phrase "wherein, if no difference between said two related nucleic acid sequences is present, branch migration in

said four-way complex continues until complete strand exchange occurs and said four-way complex resolves into two duplex nucleic acids, thereby forming a stabilized four-way complex" in step b) because the first part and the second part of this phrase do not correspond each other. Please clarify.

12. Claim 1 is rejected as vague and indefinite. Since either a first reagent or said four-way complex in step c) do not label with a dye, it is unclear how to produce a detectable signal. Please clarify.

13. Claim 6 is rejected as vague and indefinite because not all dye can bind to a four-way complex. Please clarify.

14. Claim 16 is rejected as vague and indefinite. Since said first or second reagent or said four-way complex in step a) do not label with a dye, it is unclear how to produce a detectable signal. Please clarify.

Double Patenting

15. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The

filings of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

16. Claims 1-18 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-18 of prior U.S. Patent No. 6,653,079 B2. This is a double patenting rejection.

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 1-18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,821,733 B2. Although the conflicting claims are not identical, they are not patentably distinct from each other because an obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but examined claims in this instant application are not patentably distinct from the reference claims because the examined claims are either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). Although claims 1-18 in this instant application are not identical to claims 1-21 of U.S. Patent No. 6,821,733 B2, claims 1-21 of U.S. Patent No. 6,821,733 B2 are directed to the same subject matter and fall entirely within the scope of claims 1-18 in this instant application. In other words, claims 1-18 in this instant application are anticipated by claims 1-21 of U.S. Patent No. 6,821,733 B2.

19. Claims 1-18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 6,878,530 B2. Although the conflicting claims are not identical, they are not patentably distinct from each other because an obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but examined claims in this instant application are not patentably distinct from the reference claims because the examined claims are either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). Although claims 1-18 in this instant application are not identical to claims 1-21 of U.S. Patent No. 6,821,733 B2, claims 1-22 of U.S. Patent No. 6,878,530 B2 are directed to the same subject matter and fall entirely within the scope of claims 1-18 in this instant application. In other words, claims 1-18 in this instant application are anticipated by claims 1-22 of U.S. Patent No. 6,878,530 B2. Note that detecting said stabilized four-way complex recited in claim 1 of 6,878,530 B2 is by binding detection molecule such as RuvA (see column 18).

Conclusion

20. No claim is allowed.
21. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Frank Lu
Primary Examiner
March 17, 2006

Frank Lu
FRANK LU
PRIMARY EXAMINER